

specification does not disclose DLK and LZK activity, and does not provide enablement for the treatment of a mammal susceptible to or having a neurological condition. The Examiner also states that the claims are directed to activities which are unsupported by the specification. This ground of rejection is traversed.

In order to expedite the prosecution of this application, the claims have now been amended to exclude DLK and LZK activity, and to delete the remaining language which has been objected to. Accordingly, the amended claims are now believed to be in full compliance with all of the requirements of 35 U.S.C. 112, first paragraph.

Claims 2, 7-9 and 12-13 have also been objected to under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the invention. This ground of rejection is traversed.

The claims have been amended to correct the Markush language, and to delete identical claims. In addition, the claims are now believed to overcome the objection concerning the further limitation of the claimed method.

Claims 1, 6, 14, 19 and 45 have been rejected under 35 U.S.C. 102(e) as being anticipated by Miller et al. This ground of rejection is traversed.

The Examiner states that this rejection is proper since MEKK1 phosphorylates SEK1, and that this property meets the limitation of the claims concerning an activity having the ability to bind a SEK1 protein.

Applicant notes that this limitation has now been removed from the claims. Accordingly, this rejection has been obviated.

Claim 19 also stands rejected under 35 U.S.C. 103(a) as obvious over Tibbles et al., Rana et al. and Hirai et al., each in view of Au-Young et al. This ground of rejection is also traversed.

This rejection also appears to be based on the claim limitation concerning the ability to bind a SEK1 protein. Since this limitation has been removed from the claims, this rejection has also been obviated.

In view of the foregoing facts and reasons, this application is now believed to overcome the remaining rejections, and to otherwise be in proper condition for allowance. Accordingly, withdrawal of the rejections, and favorable action on this application is solicited. Entry of this Amendment is deemed appropriate at this time since the amendments are responsive to the rejection, are a genuine attempt to advance the prosecution of the application, and do not require

any further search or consideration on the part of the Examiner. The Examiner is invited to contact the undersigned at the telephone number listed below if this is believed to facilitate allowance of this application.

Respectfully submitted,

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MARKED-UP CLAIMS

1. (Five Times Amended) A method for assessing a compound's ability to prevent neuronal cell death [occurring in a mammal susceptible to or having a neurological condition], comprising:

a) contacting a compound with cultured neuronal cells having activated MLK activity, wherein the activated MLK activity is selected from the group consisting of MLK1 activity, MLK2 activity, and MLK3 activity, and wherein the activity is a kinase activity [DLK activity, LZK activity, and an ability to bind a SEK1 protein]; and

(b) determining the number of cultured neuronal cells that die;

wherein a decreased number of dead cultured cells in the presence of the compound compared to the number of dead cultured neuronal cells in the absence of the compound is indicative of the compound's ability to prevent neuronal cell death.

2. (Three Times Amended) The method of claim 1, wherein the neuronal cells [are expressing] express a mutated protein selected from the group consisting of polyglutamine stretch-expanded huntingtin [or] and C-terminal 100 amino acids of amyloid precursor protein, or the neuronal cells are treated with a neurotoxin to induce apoptosis.

7. (Three Times Amended) The method of claim 1, wherein the neuronal cell death [occurs in a mammal having a neurological disease whereby] results from exposure of the cells to glutamate or kainic acid mediated excitotoxicity [is involved in neuronal cell death].

8. (Three Times Amended) The method of claim 1, wherein the neuronal cell death [occurs in a mammal having] results from a neurological disease [comprising] selected from the group consisting of Huntington's disease, Parkinson's disease [or] and Alzheimer's disease.

9. (Four Times Amended) A method for assessing a compound's ability to prevent neuronal cell death [occurring in a mammal susceptible to or having a neurological condition], comprising:

a) contacting a compound with cultured neuronal cells expressing a mutated protein selected from the group consisting of polyglutamine stretch-expanded huntingtin [or] and

C-terminal 100 amino acids of amyloid precursor protein, or with neuronal cells treated with a neurotoxin to induce neuronal cell death; and

(b) determining the number of cultured neuronal cells that die;

wherein a decreased number of dead cultured neuronal cells in the presence of the compound compared to the number of dead cultured cells in the absence of the compound is indicative of the compound's ability to prevent neuronal cell death.

14. (Five Times Amended) A method for assessing the ability of a compound to prevent neuronal cell death [occurring in a mammal susceptible to or having a neurological condition], comprising:

a) contacting a compound with cultured neuronal cells having activated MLK activity, wherein the activated MLK activity is selected from the group consisting of MLK1 activity, MLK2 activity, and MLK3 activity, and wherein the activity is a kinase activity [DLK activity, LZK activity, and an ability to bind a SEK1 protein];

b) contacting, in the presence of the compound, surviving cells from step (a) with an agent that induces apoptosis; and

(c) comparing the level of apoptosis in the cells in the presence of the compound with the level of apoptosis in the cells in the absence of the compound;
wherein the compound is a potentially useful drug for treating mammals when the level of apoptosis in the cells in the presence of the compound is less than the level of apoptosis in the cells in the absence of the compound.

19. (Four Times Amended) A method for assessing a compound's ability to inhibit MLK activity, comprising:

a) contacting a compound with a MLK protein and a substrate therefore, wherein the MLK protein is selected from the group consisting of MLK1, MLK2, and MLK3, [DLK, LZK] and combinations thereof;

b) measuring the level of MLK activity, wherein the MLK activity is a [selected from the group consisting of] kinase activity [and an ability to bind a SEK1 protein]; and

c) comparing the level of MLK activity in the presence of the compound with the level of MLK activity in the absence of the compound, wherein a decrease in MLK activity in

the presence of the compound is indicative that the compound has an ability to inhibit MLK activity.

45. (Amended) A method for assessing the ability of a compound to inhibit MLK activity and to prevent neuronal cell death, comprising the steps of:

a) contacting a compound with a MLK protein and a substrate therefore, wherein the MLK protein is selected from the group consisting of MLK1, MLK2, and MLK3, and combinations thereof;

b) measuring the level of MLK activity, wherein the MLK activity is a kinase activity [selected from the group consisting of an enzymatic activity, an ability to bind a SEK1 protein, and an ability to phosphorylate a SEK1 protein];

c) comparing the level of MLK activity in the presence of the compound with the level of MLK activity in the absence of the compound, wherein a decrease in MLK activity in the presence of the compound is indicative that the compound has an ability to inhibit MLK activity;

d) contacting the compound having an ability to inhibit MLK activity with cultured neuronal cells having activated MLK activity, wherein the activated MLK activity is a kinase activity [selected from the group consisting of an enzymatic activity, an ability to bind a SEK1 protein, and an ability to phosphorylate a SEK1 protein]; and

e) comparing the occurrence of apoptosis in the cultured neuronal cells in the presence of the compound with the occurrence of apoptosis in the cultured neuronal cells in the absence of the compound;

wherein the compound having an ability to inhibit MLK activity has the ability to prevent neuronal cell death when the occurrence of apoptosis in the cultured neuronal cells in the presence of the compound is less than the occurrence of apoptosis in the cultured neuronal cells in the absence of the compound.